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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/518,610

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EXAMINER

GUPTA, ANISH

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/518,610	GHANEM ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	ANISH GUPTA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,2,6-8,11,16,18 and 20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2, 6-8, 11, 16, 18, 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

1. The amendment filed, June 9, 2008 is acknowledged. Claims 2 and 7 were amended, claims 3-5 were canceled. Claims 1-2, 6-8, 11, 16, 18 and 20 are pending in this application.

#### ***Election/Restrictions***

2. Applicant's election of Group I, claims 1-8, 10, 11, 16, with the elected species of Pro-Phe-p-F-Phe in the reply filed on December 7, 2007 is acknowledged.
3. All rejections made in the previous office action and not cited herein are hereby withdrawn.

#### **New Grounds For Rejections**

4. Applicants amendment to claim 7, which makes the claim independent has necessitated the art rejection and written description rejection to shift from claim 1 to claim 7-8. Arguments have been addressed to the extent they apply to claim 7 and 8.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 7-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Pei et al.  
(US20040009956).

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The claims are drawn to a tripeptide conjugated to an active agent.

The reference discloses a phosphotyrosine mimetic conjugated to the peptide VRF (see claim 13). The peptide Val-Arg-Phe is one of the tripeptides claimed in claim 5. The non-peptide portion of the molecule meets the limitation of the pharmacologically active group. Note that the claim does not require the addition of a drug molecule but is drawn solely to tripeptides. The reference disclose a tripeptide with Phe, thereby meeting the limitation of claim 7-8.

6. Claims 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Bebbington (WO200200263).

The claims are drawn to a tripeptide conjugated to an active agent.

7. The reference disclose a tripeptide conjugated with doxorubicin. The reference specifically discloses tripeptides such as met-ala-leu and leu-ala-leu conjugated to doxorubicin. Doxorubicin is also known as adriamycin. Note that the claim does not require the addition of a drug molecule but is drawn solely to tripeptides. Thus, the reference meets the limitation of the claims.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

“To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.” Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include “level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

“A written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) (“In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . .”). Regents of the University of

California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP 2163. The MPEP states that for a genus claim, written description may be satisfied by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.. Further, the MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims recite a tripeptide comprising a proteolytic enzyme cleavable amino acid moiety. The generic statements of a tripeptide comprising a proteolytic enzyme cleavable amino acid moiety does not provide ample written description for the compounds since the claims do not define the requisite relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. Indeed the base claim does not define a single structural feature, besides the presence of an amide

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bond. The mere presence of three amino acids, to form the tripeptide, does not provide ample written guidance since one of ordinary skill in the art cannot determine which naturally or non-naturally amino acids comprise the tripeptide.

As stated earlier, the MPEP states that written description for a genus can also be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic with respect to all possible compounds and peptides encompassed by the claims. The possible structural variations are limitless to any class of drug, active agent, or active site and any tripeptide. The possible number of peptides encompassed by the claims are  $2^{20}$  or 3,486,784,401 different possibilities when only naturally occurring amino acids are used. This does not include those peptides that contain side chain modifications and/or have non-naturally occurring amino acids. The specification discloses eight tripeptides, FFP, PFF, FFS, SFF, FFN, NFF, FRV, VRF. Most of these peptides contain two Phenylalanine and are retroinverso of their counterpart. These eight tripeptides do not provide a representative number of examples for 3,486,784,401. None encompassed by the claims have modification, aside from the presence of a fluorine on the para position of the Phe residue. None of the peptides disclosed utilize any nonnaturally occurring amino acids such as Norvaline, norleucine etc.... The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the

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inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

### **Response to Arguments**

Applicants argue that the claims have been restricted to tripeptide explicitly mentioned.

Thus, the rejection should be withdrawn.

Applicants arguments have been fully considered but have not been found persuasive.

Applicants amendment to claim 7 has opened the scope of the claim to any peptide. Claim 7 is no longer dependent on claim 1 and does not include the tripeptides explicitly disclosed in the specification. Thus, the grounds for rejection are still applicable to the claim.

### **Second Paragraph Rejections**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-2, 6, 11, 16, 18, 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As amended, claim 1 is drawn to specific peptides and the claims further recites that the specific tripeptide comprises a "not terminal proteolytic enzyme cleavable amino acid moiety that is connected to a drug." It is unclear from the claim if the specific tripeptides are further modified with a "not terminal proteolytic enzyme cleavable amino acid moiety." For example, does the tripeptide have an additional amino acid on the terminal end rendering the sequence a tetrapeptide rather than a tripeptide?



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As amended, it is unclear if claim 1 is drawn solely to the tripeptide or is drawn to a complex comprising a tripeptide connected to a "not terminal proteolytic enzyme cleavable amino acid moiety" which is then connected to a drug. The preamble of the claim recites a "tripeptide." However the body of the claim is not drawn to the specifically claimed tripeptides but to tripeptides complexed with a drug. To further the confusion, claim 16 recites a pharmaceutical composition comprising a tripeptide of claim 1, thereby implying that only the tripeptide is a pharmaceutical formulation.

Claim 11 is dependent on a canceled claim 10.

Claim 7 recites the limitation "the proteolytic " in this claim. There is insufficient antecedent basis for this limitation in the claim.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.

/Anish Gupta/  
Primary Examiner, Art Unit 1654